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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,296	09/15/2005	Ales Franc	J187-028 US	1964

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,296	FRANC ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/16/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The response filed on **11/16/09** has been entered.

2. Applicant's arguments filed on 11/16/09 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-3 and 5-19 are pending in this office action. Claim 4 has been cancelled.

5. The information disclosure statement (IDS) submitted on 11/16/09 is acknowledged and has been reviewed.

6. Claims 1-3 and 5-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mckeage et al. (1995) in view of Zak et al. (US 6,503,943) and Collaueri et al. (US 6,221,393), further in view of Keppler et al. (US 5,256,653) and Calanchi et al. (US 5,900,252) as evidence by Swarbrick-Encyclopedia (1998) for the reasons made of record in Paper No. 20090617 and as follows.

Applicant again argues that "the critical issue, rather, is whether the technical solution of the combination of the excipients and the processing conditions as found in the framework of the presently-claimed invention is obvious in view of the cited references" and the "[t]he technical problem solved by the Applicant was to eliminate the problem arising during the preparation of the pharmaceutical composition containing, as active ingredients, (OC-6-43)-bis(acetato)-(I-adamantylamine)-amine-dichloroplatinic platinum complex of formula (11) (hereinafter "compound (11)") which problem was brought about by some undesirable physical properties of compound (11) (e.g., almost insoluble in water, small bulk density, small tap density, high electrostatic charge) (see paragraph [003] of the published application)".

Applicant further argues that "The person of ordinary skill would not have been motivated by the prior art or the cited references to carry out wet granulation with compound (11) for the following reasons: McKeage et al. may have mentioned similar excipients to those used for the wet granulation according the presently-claimed invention, but not in any connection with wet granulation".

"A person skilled in the art would not have anticipated or even estimated the behavior of the composition containing these excipients during the wet granulation of compound (11) and thus would not have any reasonable expectation of success".

"With regard to Collaueri, this reference teaches a wet granulation of excipients without the active ingredient, which creates the impression that the active ingredient is thus protected against severe wet granulation conditions".

In response to Applicant's argument that "[t]he technical problem solved by the Applicant was to eliminate the problem arising during the preparation of the pharmaceutical composition containing, as active ingredients, (OC-6-43)-bis(acetato)-(l-adamantylamine)-amine-dichloroplatinic platinum complex of formula" is again found not persuasive because all that is required by instant claim 1 is "a pharmaceutical composition containing..... in a mixture with at least one pharmaceutical acceptable excipient wherein it is formed of a granulate with particles smaller than 0.5.... prepared by wet granulation.... ." The Examiner has set forth a prima facie case of obviousness with the combined teachings of the prior art. The claims are not directed to solving a technical solution but merely to a "pharmaceutical composition" containing platinum complex in a mixture of at least one pharmaceutical acceptable excipient formed of a granulate with particles smaller than 0.5 mm in size. Accordingly, the combination of references are *prima facie* obvious for one of ordinary skill in the art to have used the teachings of the prior art to obtain the claim invention with a reasonable expectation of success.

It is also confusing how Applicant agrees that in trying to solve the critical problem an artisan of ordinary skill may have considered wet granulation but then contradicts himself/herself that the wet granulation carried out with the compound (ii) and any excipients would not have been realized with any reasonable expectation of success... see page 12 of response. Applicant again is incorrect that Zak does not contribute to the instant claim 1. Zak was introduced to show that inclusion of excipients to form a platinum complex were known in the prior art before filing of the instant

invention, and ties in with the teachings of Mckeage. Zak also is employed for its teaching that the platinum complex is (OC-6-43) Bis (acetato)-(1-adamantylamine)-amine-dichloroplatinum (see col. 3, lines 48-51, as required by instant claim 4). Thus compounds of claims 1 and 4 are obvious variations of instant formula I wherein the complex comprises a native saccharide, cyclodextrin that may also be modified.

In this case, the combined teachings of the prior art of record would have suggested to those of ordinary skill in the art to formulate a "pharmaceutical composition" containing a platinum complex, for the reasons made of record. McKeage specifically teach the formulation in Example I of the specification (when the specification is used as a dictionary) wherein the composition for wet granulation comprises a platinum IV complex (i.e., JM 216), a modified starch (i.e., sodium starch glycolate); microcrystalline cellulose (i.e., a poly saccharide) and lactose (see page 452 under drug). Mckeage is only lacking in the teaching that the formulation is produced by wet granulation with particles smaller than 0.5 mm. As further evidenced by Kaplan et al. (US 4,302,446, newly submitted), wet granulation of platinum IV complexes in a 0.5 mm range of particle size is (see col. 5, lines 37-41 and col. 8, lines 32-40). It should also be noted that claim 1 only requires a neutral saccharide and a modified polysaccharide (broadly). Thus any neutral saccharide and a native or modified polysaccharide when used in the composition is expected to be successful.

As to the argument that Collaueri does not teach a platinum complex, this is irrelevant in this 103 rejection, because Collaueri is used to show that granules entering into pharmaceutical compositions are advantageously prepared from a polysaccharide

having particles less than 100 µm (i.e., 0.1 mm), which is less than 0.5 mm, and therefore is alternatively relevant to the formulation, itself.

The statement that different polysaccharides are used in Collaueri is also found not persuasive because the skilled artisan would have been motivated to employ polysaccharides other than xanthum gums in a wet granulation process with a neutral saccharide and a polysaccharide, as claimed in instant claim 2, because no specific type of polysaccharide is required in instant claims 2 and 6 (for example). Applicant should also note that Collaueri teaches the composition is produced or processed by wet granulation, as stated in the last office action of record.

Thus from the evidentiary support, one of ordinary skill in the art would have substituted Mckeage's platinum IV complex with Zak's platinum complex to formulate a tablet by a wet granulation process with a reasonably expectation of success because wet granulation is used to improve flow, compressibility, bio-availability, and homogeneity of low dose blends, electrostatic properties of powders, and stability of dosage forms. One of ordinary skill in the art would have reasonably expected success in substituting Mckeage's compound JM 216 with Zak's compound ((OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum) because both compounds are used for the same treatment conditions and substituting one for the other is within the purview of the skilled artisan.

7. Claims 12-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mckeage et al. (1995) in view of Zak et al. (US 6,503,943) and Collaueri et al. (US

6,221,393), further in view of Keppler et al. (US 5,256,653) and Calanchi et al. (US 5,900,252), as evidence by Swarbrick-Encyclopedia of Pharmaceutical Technology (1998), as applied to **claims 1-11** for the reasons made of record in Paper No. Paper No. 20090617 and as follows.

The above argument and response also applies here in its entirety.

Affidavit

8. The affidavit submitted by Petr Sova under 37 CFR 1.132 filed on November 16, 2009 is insufficient to overcome the rejection of claims 1-3 and 5-19 based upon the prior art of record as set forth in the last Office action because: Zak et al teach a pharmaceutical composition for the therapy of oncological disease containing platinum complex and at least a pharmaceutical excipient wherein the modified saccharide is beta-or gamma cyclodextrin (see col. 3, lines 9-15) and Collaueri et al. teach granules entering into pharmaceuticals compositions are advantageously prepared from a polysaccharide having particles less than 100 μm which is less than 0.5 mm, wherein the polysaccharide is mixed with lactose. See col. 2, lines 56-61 and col. 5, lines 37-42. Table 1 teaches the procedure is by wetting. See col.'s 7 and 8. It is also noted that the particle size is based on the release of the active agent over the desired period of time. See col. 3, lines 34-65.

KSR Obviousness

Applicant is directed to KSR v. Teleflex, Inc., No. 04-1350 (U.S. Apr. 30, 2007), which states, "The combination of familiar elements according to known methods is

likely to be obvious when it does no more than yield predictable results. KSR v. Teleflex, Inc. 82 USPQ2d at 1395 (2007).

Additionally, "[t]he obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." KSR v. Teleflex, Inc. 82 USPQ2d at 1396 (2007).

With regard to the strict construction and application of the TSM test, Applicant is directed to KSR v. Teleflex, Inc., No. 04-1350 (U.S. Apr. 30, 2007), which states, "rejections on obviousness grounds cannot be sustained by mere conclusionary statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." (KSR, slip op. at 14). The Court continued, stating that "helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." KSR, slip op. at 15. As such, the rejection at issue and its analysis under 103(a) meets all of the *prima facie* requirements under Graham v. Deere (1966) (*supra*) and KSR v. Teleflex (2007) (*supra*).

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
1/19/10

/Robert C. Hayes/
Primary Examiner, Art Unit 1649